INCIDENCE RATE OF SUBSTITUTIONS DUE TO TENOFOVIR DISOPROXIL FUMARATE RELATED BONE AND RENAL TOXICITY AND AMONG ADULTS ATTENDING THE INFECTIOUS DISEASES INSTITUTE KAMPALA.

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Background

Lifelong antiretroviral therapy may lead to toxicities that increase patient morbidity and may prove costly to the health system. Drug substitutions are a recognized strategy for managing antiretroviral toxicities. The World Health Organization (WHO) recommends tenofovir disoproxil fumarate (TDF)-based regimens as preferred first-line regimens but TDF is associated with bone and renal toxicity and data is scarce on these toxicities in sub-Saharan African countries [1,2]. We report the incidence rate and factors associated with TDF-based regimen substitutions due to toxicities among adults attending an HIV clinic in Uganda.

Methods

A retrospective case-control analysis was conducted among adults attending the Infectious Diseases Clinic in Uganda between 1st January 2005 and 31 December 2017. Adults who had had a substitution to their TDF based regimen due to TDF bone and renal toxicity were included as cases. Controls were randomly selected (1:3) and frequency matched to case patients by age, gender and duration on TDF-based regimen. We determined the incidence rate and summarized patient demographics using medians, frequencies and percentages. Patient characteristics were compared using chi-square tests and Wilcoxon signed rank tests. Logistic regression was performed to explore associations between baseline covariates and the odds of substitution of TDF due to bone and renal toxicities.

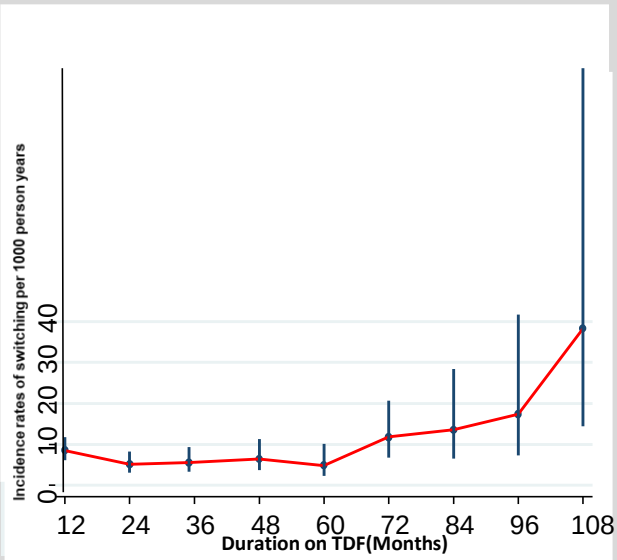
Results

From 24 – 60 months of TDF exposure, incidence rate was <4 per 10,000 per person-years (ppy) but this increased to >9 per 10,000 ppy after 72 months of exposure. Compared to the controls, in univariate analyses, cases were more likely to have advanced disease (WHO Stage III-IV) and have lower CD4 counts but other baseline characteristics were similar (Table 1). In multivariate analyses, patients at WHO stage III and IV at ART initiation had greater odds of switching from TDF based regimen due to toxicity compared to those who were in WHO stage I and II (OR, 95%CI, p-value: 2.12, 1.25-3.55, 0.004). Higher CD4 at ART start was protective of switching (OR, 95%CI, p-value: 0.94, 0.89-0.98; 0.017). However we did not find any association between odds of substitution and other baseline characteristics (Table 1).

Table1: Patient's Characteristics at baseline

Characteristics	Cases (n=113)	Controls (n=339)	P value
Male sex, %	42.48	44.31	0.736
Age, median (IQ-range)	42.1 (35.00-51.20)	41.50 (34.8-49.10)	0.57
BMI, %			0.584
Underweight (<18.5)	20.19	18.95	
Normal (18.5-24.9)	60.58	56.86	
Overweight (>25)	19.23	24.18	
WHO Stage (%)			<0.0005
I-II	42.48	61.58	
III-IV	57.52	38.15	
CD4 count median (range)	166 (41-352)	238 (87-462)	0.005
ART duration before exposure to TDF	0.5 (0-36.60)	0 (0-34.30)	0.22
ART duration on TDF	43.15 (10.82-96.69)	51.51 (17.71-84.66)	0.20
History of TB (%)	10.62	7.38	0.22
Hypertension (%)	6.19	11.69	0.10
Diabetes (%)	1.77	2.46	0.67
NSAIDS use (%)	46.02	46.46	0.94
History of renal disease (%)	0.00	0.62	0.400

Fig1:Incidence rates of switching from TDF to ABC or ZDV



Conclusions

Incidence of toxicities increased more than two-fold after 5 years of TDF exposure. Furthermore, patients with advanced disease had greater odds of a switch for toxicity. Clinicians should remain vigilant for TDF toxicity in otherwise stable patients on TDF-based regimens and among patients with advanced disease

References

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2. World Health Organization: Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach – 2nd ed.2016; 2016